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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,363	04/15/2007	Elaine Alison Irving	PB60024USw	6175

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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
05/06/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/550,363	IRVING ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 17-19* is/are rejected.

7)☒ Claim(s) *8-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/19/05, 8/26/08, 4/21/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 29 May 2009 have been entered. Claims 1 and 3 - 19 are pending and under examination.

Information Disclosure Statement

2. The information disclosure statements have been considered. Note that several references on the IDS filed 19 September 2005 have been crossed out. These references have not been considered as no copies were provided. Note that while reference 2004/0002790, cited on page 3 of the IDS filed 26 August 2008, has been considered, it is not immediately obvious how that reference pertains to the presently-claimed methods.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

The examiner notes that the U.K. foreign priority document fails to disclose SEQ ID NO:18 and SEQ ID NO:19. Therefore claims 17 - 18, which are limited to methods of administering proteins with these particular sequences, do not receive benefit of the foreign priority document. The effective filing date of claims 17 and 18 is 2 February 2004, the date that PCT/EP04/01016 was filed.

Claim Objections

4. Claims 1 and 17 - 19 are objected to because of the following informalities:

Claim 1 recites the abbreviation "MAG" without first spelling out the name of the protein. The claim should be amended to recite the full name of the protein prior to using the abbreviation.

Claims 17 and 18 each recite "wherein the antibody heavy chain is SEQ ID NO:18" and "wherein the antibody light chain is SEQ ID NO:19" respectively. A protein cannot be a sequence; rather a sequence is a property of a protein. To reflect more conventional claim language and to clarify that applicant is claiming methods of using antibodies rather than methods of using sequences of letters, it is suggested that the claims be amended to replace the word "is" with the phrase "has the amino acid sequence of". Claim 19 is confusing because it refers to "the antibody having the CDRs of claim 6", but claim 6 is directed to a method, not an

antibody or CDRs. It is suggested that applicant amend claim 19 to recite the specific CDRs. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3 - 7, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering anti-MAG antibodies, does not reasonably provide enablement for administering any and all functional fragments as recited in claim 1 or for administering any and all altered antibodies as recited in claim 3, or for administering antibodies wherein only one of the CDRs is specified, as in claims 6-7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In the present case, the nature of the invention is complex. The claims are drawn to improving biological processes (promoting oligodendrocyte survival) in human patients suffering from stroke. The claims are broad in that they encompass not only administering antibodies which bind to MAG, but also encompass administering antibodies that are "functional fragments", with no limit on what constitutes a fragment or what function is to be retained in said fragment, as well as "altered antibod[ies]". Furthermore, claims 6-7 encompass administering antibodies that need only have a single CDR, even though it is well-understood in the art that all six CDRs are required in order for an antibody to bind its antigen.

With regard to the issue of administering antibodies having less than the full set of six CDRS, the specification discloses only antibodies that contain both variable heavy chain (HCVR

or V_H) and variable light chain (LCVR or V_L) regions with no less than 6 CDRs, 3 from the V_H chain and 3 from the V_L chain that bind to antigen. The specification does not enable antibodies or a "functional fragment thereof", which do not contain the full set of 6 CDRs, although the claims encompass such variants which lack one or more CDRs.

It is well established in the art that the formation of an intact antigen-binding site of all antibodies generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs, or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope (Paul, Fundamental Immunology, 1993, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions"). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation are required in order to produce a protein having antigen-binding function, and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites (Paul, page 293, first column, lines 3-8 and line 31 to column 2, line 9 and lines 27-30). In other words, all three CDRs of the heavy chain variable region and all three CDRs of the light chain variable region are important for determining the ability of an antibody to bind antigen. For example, Padlan et al. (*Proc Natl Acad Sci USA*, 1989; 86:5938-5942) describe the crystal structure of an antibody-lysozyme complex where all 6 CDRs contribute at least one residue to binding and one residue in the framework is also in contact with antigen (see entire document, but especially page 5940, right column, section under "Structure of the Combining Site"). Thus, the state of the art recognizes that it would be highly unpredictable that an antibody comprising less than all six CDRs from an antibody with a desired specificity would bind the same antigen. Hence, it is unlikely that the antibodies and fragments thereof as defined by the claims, which may contain less than the full complement of CDRs from the heavy and light chain variable regions, or fragments which may not comprise the framework regions, variable regions and/or CDRs in the correct order or three-dimensional conformation, have the required binding function. In fact, the art recognizes that simply having one CDR from those listed in claims 6 and 7 does not indicate that the antibody will bind to MAG. For example, Ni et al. WO 99/55735 teach mAb163-93, an antibody which comprises present SEQ ID NO:2 but binds to G-CSF receptor. Applicants have provided

insufficient evidence or nexus that would lead the skilled artisan to predict the ability of producing an antibody and fragments thereof containing fewer than 6 CDRs, resulting in an antibody that retains the antigen specificity currently claimed.

With respect to the "functional fragment thereof" recited in claim 1, there is no limit on what constitutes a fragment, and there is no limit on what function this fragment must have. While claim 6 recites "functional fragment", that claim explicitly requires that the fragment bind MAG. Claim 1, by contrast, does not require such binding for the fragment. Thus claim 1 reads on administering any and all fragments of antibodies, with any and all functions, for treatment of stroke in humans. The specification fails to provide working examples or guidance commensurate in scope with the full breadth of "functional fragment" of antibodies to be administered. Therefore the skilled artisan would have to discover, on his or her own, which structures are necessary or sufficient for the claimed methods to work. Given the breadth of the claims and the lack of disclosure of working examples or guidance commensurate with the full scope of the claims, one of skill in the art would have to resort to an unduly large degree of experimentation in order to make and use the claimed invention. Similarly, there is insufficient guidance as to what constitutes an "altered antibody" as recited in claim 3 and encompassed by claim 1. A skilled artisan could not carry out the full scope of the claimed methods in the absence of undue experimentation.

In order to advance prosecution, it is recommended that applicant delete the words "or a functional fragment thereof" from claim 1, cancel claim 3, and amend claims 6-7 to require that all six CDRs be present. Note claim 19 is included in this rejection as well. Since it requires administering an antibody which binds to the same epitope as claim 6, claim 19 includes methods of administering antibodies which have only one CDR and therefore is not enabled over its full scope for at least the same reasons.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3 - 7, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Irving WO 02/062383, published 15 August 2002.

Irving teaches administering antibodies that bind to MAG for treatment of stroke, as recited in claim 1. See for example Irving p. 2 line 36 - p. 3 line 8, and lines 20 - 23 which specifically list humans as the patients to be treated. Irving also teaches altered antibodies, as in claim 3, specifically chimeric and humanized antibodies as in claims 4-5. See for example p. 4 line 5 - 19, page 7 lines 10 - 16, and p. 7 line 36 - p. 8 line 7. Therefore the publication by Irving anticipates each of claims 1 and 3-5. Irving teaches that preferably the antibodies administered for treatment of stroke comprise one or more CDRs selected from those listed at p. 4 line 34 - p. 5 line 10. Irving's CDRs L1 and H3 are identical to applicant's SEQ ID NO:1 and 6 respectively, thereby anticipating claims 6 and 7.

Claim 19 is anticipated as well. Although the reference by Irving does not explicitly teach whether the antibody which comprises SEQ ID NO:1 and 6 binds to the same epitope as an antibody comprising SEQ ID NO:1-6, as required by claim 19, since the prior art antibody shares considerable identity (note that while the other CDRs are not identical they are very close in sequence; compare SEQ ID NO:1-6 with the sequences listed on p. 5 of Irving) it is presumed to bind to the same epitope absent evidence to the contrary.

7. Claims 17 - 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Ellis (U.S. Patent 7,612,183, issued 3 November 2009, PCT filed 5 August 2003.

Applicant is reminded that claims 17-18 do not receive the benefit of the foreign priority document as they recite features which were not disclosed in that document. As set forth above, the effective filing date of these claims is 2 February 2004.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Ellis teaches SEQ ID NO:30, which is identical to applicant's SEQ ID NO:18, and SEQ ID NO:31, which is identical to applicant's SEQ ID NO:19. These are disclosed as being heavy and light chains of anti-MAG antibodies respectively, and are to be used for treatment of stroke. See for example Figure 5 (disclosing the sequences) as well as column 4 lines 36-51 (disclosing methods of administering the antibodies disclosed in the invention).

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-7, and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 13-16 of copending Application No. 11/746355. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case they encompass administration of antibodies that bind to MAG and comprise SEQ ID NO:1 and 6 to patients with stroke.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. Claims 1, 3-7, and 17-19 are rejected.

10. Claims 8-16 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
May 3, 2010